Wolfram Hörz 1944–2005

Fields of research are frequently cultivated by a few scientific entrepreneurs whose vision and drive inspire the rest of us. The analysis of chromatin structure and function has profited immensely from leaders such as Wolfram Hörz. The yeast *PHO5* promoter model developed by Wolfram Hörz has become a paradigm for dissecting the events underlying promoter-specific chromatin opening in response to environmental cues. His elucidation of such events has yielded reference points for numerous followup studies investigating the emerging principles of gene regulation through chromatin reconfiguration. Wolfram Hörz died on November 13, 2005 from colon carcinoma and associated metastases. The news of his premature death found many of his colleagues unprepared for this loss. The field of chromatin remodeling has lost not only one of its scientific leaders but also an unusually amiable colleague.

Wolfram Hörz was born in Nürtingen, a small town in Southern Germany, on April 4, 1944. His parents were teachers at the local high school that Wolfram and his brother attended. Guided by his talent and perhaps the example of his brother and uncle, who had become medical doctors, Wolfram chose to study medicine at a local traditional university, the University of Tübingen, in 1963. He passed all of the preclinical medical exams with top grades and then decided to widen his horizons. During a semester in Vienna, his intense studies were alleviated by frequent visits to the opera. The next six months found him studying in Hamburg, perhaps hoping that he would find time for the occasional sailing trip. Although his medical studies were very successful, he felt increasingly pulled toward research. He obtained a Fulbright fellowship in 1966, which supported his biochemistry studies at Duke University in Durham, North Carolina. It was here that he met his future wife, Welda. In 1968 she planned a six month study visit to Germany and wanted to learn more from the German student about his home country. Wolfram generously shared his knowledge, and soon she regretted her commitment to the six month trip, wishing instead that she had stayed in Durham. During the following months of intense correspondence, they realized that they were meant for each other, and they married in 1969.

Wolfram Hörz
Photo courtesy of Dr. Gustav Klobeck.

Wolfram pursued a PhD in biochemistry on the initiation of translation in reticulocyte extracts, under the guidance of Kenneth McCarty at Duke University. As he wished to continue his studies on RNA translation, he applied for a position in the laboratory of Hans G. Zachau, who was known for his work on tRNA structure and metabolism. Wolfram Hörz's credentials were excellent, and he was welcomed into Zachau's München laboratory in 1971.

I think it is fair to say that Wolfram made his scientific living studying the interactions of proteins with nucleic acids using nuclease digestion assays. Initially he probed the interaction of aminoacyl-tRNA synthetases with tRNA but soon discovered that chromatin was an equally interesting substrate. Back then the structure of chromatin was a complete mystery. Histone proteins were known to be the most abundant constituents of chromatin, and nuclease digestion experiments hinted at some kind of repetition in chromatin organization. Yet, it was not until 1974 that nucleosomes were described as the dominant structural feature of chromatin. Hörz, Zachau, and their colleagues established an extensive track record probing chromatin structure, including the elucidation of satellite heterochromatin and metaphase chromosomes using various types of nucleases. Wolfram received tenure as a staff scientist at the University of München in 1979, became associate professor in 1982, and became full professor in 1991.

As an independent investigator, Hörz expanded his analyses of chromatin structure in two important ways. First, he began to reconstitute nucleosomes

in vitro to learn about the rules that govern their positions in chromatin. Together with his PhD student, Winfried Linxweller, he reported in 1985 that sequence-specific interactions between histones and DNA form the basis for the regular repeated pattern of nucleosomes in mouse satellite DNA (Linxweller and Hörz, 1985). Second, he applied the fairly new method of mapping promoter structure using DNase digestion and indirect end labeling (DNase-hypersensitive site mapping) to the yeast *PHO5* promoter. The results reported in the EMBO journal in 1986 (Almer et al., 1986) documented that removal of positioned nucleosomes from the yeast *PHO5* promoter upon induction of the phosphate-regulated *PHO5* gene resulted in release of additional upstream activating DNA elements. This was one of the first descriptions of nucleosome remodeling. The phenomenon proved to be a fundamental discovery and stimulated many other investigators to engage in similar research. Wolfram and his team spent the next 20 years, until his death, investigating the molecular mechanisms that underlie nucleosome remodeling at the promoters of phosphate-regulated genes in yeast. With modest resources, relentless focus, and a passion for detail, Wolfram and his group systematically analyzed the requirements for chromatin remodeling events, including DNA sequences, transactivating factors, and regulators of chromatin structure. Their observation that the remodeling event was independent of replication pointed to a dynamic transition in chromatin structure during interphase of the cell cycle (Schmid et al., 1992). The finding that recruitment of a polymerase complex was able to trigger opening of a promoter's chromatin—a collaborative effort with the Ptashne laboratory (Gaudreau et al., 1997)—suggested that the participating activities not only worked synergistically but also were linked through the coordination of physical interactions. Paying attention to subtleties in the data paid off. After it became clear that histone acetylation was required for nucleosome remodeling—a collaboration with the Berger laboratory (Gregory et al., 1998)—a careful, time-resolved analysis revealed that acetylation was only transiently required as a stepping stone on the path toward chromatin opening (Reinke et al., 2001).

When I joined the München department in 1999, we had just discovered that nucleosomes could be induced to move along DNA in vitro and strongly advocated a model in which access to nucleosomal DNA could be generated simply by sliding intact histone octamers off of a target site. Wolfram never considered this an option for the yeast *PHO5* promoter. After all, his group had observed the concerted remodeling of four consecutive nucleosomes upon induction of the *PHO5* promoter. Considering the density of nucleosomes in yeast chromatin, it was not clear where these four nucleosomes could slide. Of course, Wolfram was right. Almost 20 years after the initial observation of the removal of positioned nucleosomes, Reinke and Hörz (2003) proved that those nucleosomes were indeed evicted.

The vision, the commitment, and the perseverance of Wolfram Hörz have influenced and inspired many who work in the ever expanding field of chromatin structure and function. His critical advice, which he shared generously during private conversations or more officially as a member of the Editorial Board of *Cell* (since 1997) provided valuable guidance and quality control. Wolfram was an elected member of the European Molecular Biology Organization (EMBO), a spokesperson for local and European research networks, and a founding member of the European Network of Excellence for The Epigenome in 2003. Yet for those who looked forward to meeting Wolfram at the many international conferences to which he was invited, it was not because he was an influential leader in the field, but rather because he was such a charming and caring person. Young colleagues would seek his advice not only about scientific research but also about private matters, and he would always find time to listen. His dry humor was cordial and never cutting.

Perhaps paradoxically, one of the reasons why Wolfram appeared so amiable as a scientist was because science was not the most important aspect of his life. At any given time during his career, his family was still more important to him. No matter how busy he was, he always found time for his beloved wife, Welda, and his three children Michael, Susanne, and Anne (born in 1973, 1976, and 1981, respectively). This explains why many of us received email messages from Wolfram that were sent long after midnight. When all the homework was done and the children were in bed, he found the time to attend to business related to his "extended family," the members of his laboratory. For those of us who were fortunate enough to work closely with him, he was indeed much more than just a respected colleague but rather a fatherly mentor and a dear friend.

Wolfram Hörz was content with his life. Diagnosed with colon cancer in 2001 and realizing that time was running out, he did not rush off to see the world but instead chose to continue his normal routine, including long hours in the lab, and to spend extra time with his family. There was nothing he wanted to change. His last joy was holding his grandchild, born in September 2005. I will remember Wolfram Hörz with great affection, gratitude, and respect. He will remain a role model for many of us, not only because of his scientific achievements, but because his scientific excellence was blended with an unusually humane and caring attitude toward the people he lived and worked with.

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